

# Intensive care management of Guillain-Barre syndrome: A retrospective outcome study and review of literature

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## Abstract

**Introduction:** Guillain-Barre syndrome (GBS) is an immune mediated disorder which is associated with demyelination of peripheral nervous system and progressive muscle weakness. Severely affected patients have respiratory dysfunction and may need ventilatory support which can cause significant morbidity and mortality. There is limited Indian data with regards to the outcome of severely affected GBS patients. The present study reflects the intensive care management of severely affected GBS patients at neurological centre of a tertiary care institute of India. **Materials and Methods:** The study was designed to retrospectively review the patient records who were admitted to neurological intensive care unit (ICU) of AIIMS, New Delhi. The epidemiology, clinical features, course of management and outcome of GBS patients admitted between April 2000 to December 2005 were recorded and analysed. **Results:** The data of 59 patients were available for inclusion in the study. The mean age of patients admitted to neurological ICU was 35 years with male preponderance. Ventilatory failure was the most common indication for ICU admission. 95% patients required ventilatory support for a mean duration of 30 days. The mortality data included 60 patients and 13 patients died during the course of management. **Conclusions:** The present study indicates that severely affected GBS patients may need prolonged mechanical ventilation. Despite management in a specialized neurological ICU the mortality can be as high as 21%.

**Key words:** Critical care, Guillain-Barre syndrome, management

## INTRODUCTION

Guillain-Barre syndrome (GBS) is a demyelinating disorder of the peripheral nervous system, which is monophasic (single peak) with spontaneous remission.<sup>[1]</sup> The syndrome is an immunopathy with an acute, often fulminant evolution of demyelinating inflammatory polyradiculopathy.<sup>[2]</sup> The syndrome was first described by French neurologists Guillain-Barre and Strohl in 1916 in two soldiers with acute areflexic paralysis followed by recovery.<sup>[3]</sup>

Population based studies suggest a crude average annual incidence of rates from 0.4 to 1.7/100,000 population. Incidence is higher in males than females as well as in older (age > 60 years) compared with younger people (age < 18 years).<sup>[4]</sup> The occurrence rate is higher for white than for blacks.<sup>[1]</sup> A number of triggering factors have been implicated to be associated with GBS, 2-4 weeks before the onset of weakness.<sup>[4]</sup> They include viral, bacterial and spirochetal infections, surgery and vaccinations.<sup>[5]</sup>

The basic disease process in GBS is immunologic.<sup>[6]</sup> Antibodies directed against peripheral nerve tissue damage peripheral myelin and Schwann cells.<sup>[5]</sup> Axonal damage is thought to be secondary, but primary axonal involvement has also been reported.<sup>[7]</sup> Consequently GBS has been subdivided into the clinical variants - acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN).<sup>[5]</sup>

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Progressive motor weakness of more than one limb and areflexia are the two features required for the diagnosis of GBS.<sup>[8]</sup> Relative symmetry with mild sensory symptoms, cranial nerve involvement, autonomic dysfunction, albuminocytologic dissociation and electrodiagnostic features support the diagnosis. Classic GBS has an acute onset with progression over 10-12 days before a plateau is reached, followed by gradual recovery.<sup>[9]</sup> The devastating course may make the patient bedridden and on a respirator within 2-3 days. Respiratory dysfunction in GBS is caused by phrenic nerve involvement and loss of motor innervation to intercostals, abdominal and accessory respiratory muscles.<sup>[10]</sup>

Specific management of GBS is that of immunomodulation - plasmapheresis, intravenous immunoglobulin (IVIG) and/or steroids.<sup>[1]</sup> Ventilatory care is important in severely affected individuals. General intensive care unit (ICU) measures include physical therapy, chest physiotherapy, eye care, bowel and bladder care, positioning and padding to prevent bed sore formation, adequate nutritional supplementation and psychological support.

The outcome of GBS has varied widely in published series, with mortality rates between 1% and 18%.<sup>[11]</sup> In patients requiring mechanical ventilation, the mortality rate may reach up to 15-30%.<sup>[1]</sup> Although the outcome is generally considered to be good, 15% of survivors have some disability and 5% remain severely disabled.<sup>[12]</sup> In one survey, only 67% of patients had complete recovery after 12 months, and 20% were still significantly disabled after that period.<sup>[13]</sup> Of these, patients employed before their illness, 60% were able to return to their previous job, 25% found less demanding work and 15% did not return to work.<sup>[14]</sup> A total of 3% of patients are estimated to experience one or more acute relapses after complete or nearly complete recovery.<sup>[15]</sup> Morbidity and mortality are more frequent in severely affected patients and prognosis tends to improve with wider availability of specialized ICU management and adequate techniques for airway protection and ventilation.<sup>[11]</sup>

In a study by Winer *et al.*, one year follow-up revealed mortality of 13%, while in Massachusetts General Hospital study only 6% had died.<sup>[13,16]</sup> The reduced mortality may largely be attributed to the fact that all the patients were largely treated in a specialized neurological ICU.

Despite advances in the management and specific treatment of GBS, mortality and morbidity occurs mainly in patients with neurologically severe disease, that is., the patients who require ventilatory support and ICU. The aim of this study was to retrospectively record the clinical and outcome characteristics of the severely affected GBS patients admitted to the neurologic ICU at All India Institute of Medical Sciences, New Delhi.

## MATERIALS AND METHODS

The study was conducted retrospectively on the patients admitted to the neurology ICU between April 2000 and December 2005 with the diagnosis of GBS. The available records of all the patients were reviewed and based on electrophysiological studies and clinical features, the patients were reclassified as acute inflammatory demyelinating AIDP, AMAN, AMSAN or Miller-Fisher syndrome.<sup>[5]</sup> The characteristics of patients with GBS and follow-up data were noted.

The epidemiological characteristics and clinical features of the patients were recorded. The clinical parameters of the central nervous system included higher mental functions, cranial nerve assessment, bulbar dysfunction, motor and sensory functions, reflexes, speech and sphincter involvement. The hemodynamic alterations were noted. The respiratory characteristics recorded were respiratory rates, breath holding time, single breath count, presence of secretions and crepitations and episodes of dyspnea.

The investigation charts of the patients were screened. Abnormal variables were defined<sup>[17]</sup> and noted.

1. Anemia: Hemoglobin <10 mg/dl and/or hematocrit <30%
2. Leukocytosis: Increase in total leucocyte count more than 15,000 cells per cumm
3. Increased erythrocyte sedimentation rate (ESR): Increase in ESR was considered if the values in the first hour were more than 20% of the normal values (20 mmHg)
4. High blood urea: Increase in blood urea level more than 50 mg%
5. Abnormal liver enzymes: Increase in serum aminotransferases to more than 50 units/L
6. Hypernatremia: Serum sodium levels more than 145 mEq/L
7. Hyponatremia: Serum sodium levels <130 mEq/L
8. Hyperkalemia: Serum potassium levels more than 5 mEq/l
9. Hypokalemia: Serum potassium levels <3 mEq/l
10. Hypocalcemia: Serum calcium <8 mg/100 ml
11. Hypoproteinemia: Serum proteins <5.5 mg/dl
12. Hyperglycemia: Random blood sugar more than 120 mg/dl and/or postprandial values more than 180 mg/dl
13. Haematological abnormality: Abnormal prothrombin time, international normalized ratio and/or platelet counts
14. Growth on culture: Growth of organism (s) on tracheal, blood and urine culture (s)
15. Chest radiograms: The chest X-rays were reviewed by senior residents of neuroradiology department and any abnormality were noted.

**Management**

The management of GBS patients was noted under two headings - specific and supportive.

**Specific management**

The patients who underwent plasma exchange, immunoglobulin and/or steroids were categorized under specific management.

**Supportive management**

The various forms of supportive care were noted.<sup>[1]</sup> The patients who had respiratory dysfunction, who required intubation and tracheostomy were noted. The form and duration of ventilatory support were also recorded.<sup>[2]</sup> The use of antibiotics, antacids, sedation, analgesics, antihypertensive medication and inotropic support were also noted.<sup>[3]</sup> The use of enteral and parenteral nutrition were also reviewed.

**Course and outcome**

**Complications:** The various systemic complications that were recorded during the ICU stay of the patients included respiratory complications, gastrointestinal disorders, electrolyte imbalance, autonomic dysfunction, pain, bed sore, deep vein thrombosis and urinary tract infection.

**Outcome:** The course of ICU stay and short term outcome of the patients were reviewed in following terms: Duration of ICU and hospital stay, maximum motor disability (nadir) during ICU stay, number of patients discharged from the hospital, motor power at the time of discharge, presence of tracheostomy tube at time of discharge, oral/Rhyle’s tube feeding at time of discharge and number of patients who died during the course of ICU management.

**Statistical analysis**

The data was analyzed statistically and the values were expressed in terms of number, percentage, mean ± standard deviation or as median.

**RESULTS**

Seventy-four patients were admitted to the neurological ICU between April 2000 and December 2005. However, records were available for 59 patients only. Consequently, 59 patients were included in the study. The mortality data of one of the patients whose file was missing could be retrieved and consequently the mortality data is representative of 60 patients. The mean age of the patients was 35 years. The incidence of GBS among male patients was three times of those in female patients. AIDP was the most common form of GBS. Miller-Fisher variant of GBS was seen in one patient [Table 1].

Fever was the most common preceding illness followed by diarrhea and upper respiratory tract infection. The

median time to onset of symptoms of GBS following the preceding event was 10 days. GBS was seen following pregnancy in one patient.[Table 2]. Ninety-eight percentages of the patients had limb weakness as the presenting symptom, followed by dyspnea, bulbar and sensory symptoms. The onset of dyspnea necessitated early admission to the hospital [Table 3].

Weakness of the lower limbs was the most frequent sign on admission with 91.5% of the patients having lower limb power <4. Impaired gag and ineffective swallowing were the most common bulbar signs [Table 4a]. Majority of patients had reduced muscle tone [Table 4b]. Half of the patients were dyspneic on admission. Hemodynamic instability was seen in 11 (18.5%) patients and cardiac arrest due to autonomic dysfunction occurred in 5 (8.5%) patients [Table 4b]. The most common associated illness was hypertension [Table 5].

**Table 1: Epidemiological characteristics**

Variable	Values
Age (years)*	35.4±17.3 (11-79)
Male patients	43 (72.9)
Female patients	16 (27.1)
Indication for ICU admission	
Ventilatory failure	54 (91.5)
Others	5 (8.5)
Form	
AIDP	37 (62.7)
AMAN	13 (22)
AMSAN	4 (6.7)
Miller-Fisher syndrome	1 (1.7)
Uncertain	4 (6.7)

Values are number (%) of patients. \*Mean±SD (range). SD = Standard deviation, AIDP = Acute inflammatory demyelinating polyradiculoneuropathy, AMAN = Acute motor axonal neuropathy, AMSAN = Acute motor sensory axonal neuropathy, ICU = Intensive care unit

**Table 2: Preceding events**

Events	Values
Fever	25 (42.4)
URTI	8 (13.6)
Diarrhea	10 (16.9)
Abdominal discomfort	3 (5.1)
Pregnancy	1 (1.7)
Abortion	2 (3.4)
Others	9 (15.2)
None	17 (28.8)
Duration between preceding events and onset of symptoms (days)*	10 (2-90)

Values are number (%) of patients. \*Median (range). URTI = Upper respiratory tract infection

**Table 3: Symptoms prior to admission**

Symptoms	Number of patients (%)	Median time (range) onset of symptoms to admission (days)
Limb weakness	58 (98.3)	4 (0-26)
Sensory symptoms	23 (39)	3.5 (0-15)
Tingling	13 (22)	
Numbness	9 (15.3)	
Ataxia	1 (1.7)	
Pain	7 (11.9)	4.5 (0-8)
Bubar symptoms	27 (45.8)	2.0 (0-17)
Sphincter disturbance	6 (10.2)	1.0 (0-4)
Dyspnea	28 (47.5)	1.0 (0-30)

**Table 4a: Signs on admission to ICU**

Signs(s)	Number of patients (%)
Ophthalmoplegia	07 (11.9)
Partial	03 (5.1)
Complete	04 (6.8)
Ptosis	04 (6.8)
Facial weakness	47 (79.7)
Bulbar signs	35 (59.3)
Ineffective swallowing	13 (22.0)
Ineffective cough	2 (3.4)
Multiple affections	7 (11.9)
Abnormal sensory findings	18 (30.5)
Abnormal speech	25 (42.4)
Sphincter involvement	10 (16.9)
Abnormal pupillary sign	7 (11.9)

ICU = Intensive care unit

Electrolyte imbalance in the form of hypokalemia and hyponatremia was the most frequent investigatory finding. About one-third of the patients had anemia, leukocytosis, increased ESR values and blood urea levels [Table 6]. Abnormal hematological finding in the form of increase in prothrombin time was seen in 6 (10.2%) patients. The most common respiratory infections were with *Pseudomonas aeruginosa* and *Acinetobacter* strains [Table 7].

Intravenous immunoglobulins were most frequently used for treatment of GBS. Eleven patients received dual treatment of plasmapheresis or IVIG along with methylprednisolone [Table 8]. Most of the patients required antibiotics. Seventy-three patients required sedation during the stay at ICU. Benzodiazepines alone or in combination with opioids were commonly used [Table 8].

**Table 4b: Signs on admission to ICU**

Sign(s) Motor power	Values	
	Upper limb	Lower limb
0	12 (20.3)	20 (33.9)
1	8 (13.6)	8 (13.6)
2	11 (18.6)	12 (20.3)
3	11 (18.6)	14 (23.7)
4	15 (25.4)	4 (6.8)
5	2 (3.4)	1 (1.7)
Sign(s)	Values	
Muscle wasting	5 (8.5)	
Reduced muscle tone	54 (91.5)	
Reflexes		
Normal	4 (6.8)	
Decreased	17 (28.8)	
Absent	38 (64.4)	
Respiratory features		
Dyspnea	30 (50.8)	
Respiratory rate* (per minute)	23 (14-40)	
Breath, holding time* (seconds)	15 (5-28)	
Single breath count*	13.5 (3-105)	
Secretions	11 (18.6)	
Crepitations	10 (16.9)	
Hemodynamic alterations	5 (8.5)	

Values are number (%) of patients. \*Median (range). ICU = Intensive care unit

**Table 5: Associated illness**

Illness	Number of patients (%)
Cardiac disease	3 (5)
Hypertension	6 (10.2)
Diabetes mellitus	2 (3.4)
Gastrointestinal disorders	4 (6.8)
Malignancy	1 (1.7)
Systemic sclerosis	1 (1.7)
Epilepsy	1 (1.7)
Others	1 (1.7)

Ventilatory support was required in 56 patients. Five patients were intubated prior to admission in our hospital. Of these, 2 underwent tracheostomy before being shifted to our hospital. The median time to intubation following the onset of symptoms was 6 days while the mean duration of ventilation was 30.3 days. Nineteen patients could be extubated, while 33 patients underwent tracheostomy during ICU stay. The median interval between intubation and tracheostomy was 18 days [Table 9].



**Table 6: Investigatory findings**

Feature(s)	Number of patients (%)
Anemia	18 (30.5)
Leukocytosis	18 (30.5)
Increased ESR	18 (30.5)
Increased blood urea	21 (35.6)
Abnormal liver enzymes	15 (25.4)
Hypernatremia	5 (8.5)
Hyponatremia	21 (35.6)
Hyperkalemia	2 (3.4)
Hypokalemia	23 (39.0)
Hypocalcemia	8 (13.6)
Hypoproteinemia	10 (16.9)
Hyperglycemia	8 (13.6)
Abnormal hematology	6 (10.2)

ESR = Erythrocyte sedimentation rate

**Table 7: Growth of organisms on culture**

Site/organism	Number of patients (%)
Tracheal	23 (39.0)
<i>P. aeruginosa</i>	13 (22.8)
<i>Acinetobacter</i> species	10 (17.5)
Gram positive cocci	3 (5.3)
<i>E. coli</i>	3 (5.3)
SA	2 (3.3)
<i>P. mirabilis</i>	1 (1.7)
Gram-negative bacilli	1 (1.7)
Blood	6 (10.2)
Methicillin resistant SA	2 (3.3)
Coagulase -ve <i>staphylococcus</i>	2 (3.3)
<i>P. aeruginosa</i>	1 (1.7)
<i>Enterococcus</i>	1 (1.7)
Urine	13 (22.0)
<i>E. coli</i>	5 (8.5)
<i>K. pneumonia</i>	3 (5.3)
<i>P. aeruginosa</i>	2 (3.3)
Gram-negative bacilli	2 (3.3)
<i>P. mirabilis</i>	1 (1.7)

SA = *Staphylococcus aureus*, *E. coli* = *Escherichia coli*,  
*P. aeruginosa* = *Pseudomonas aeruginosa*,  
*P. mirabilis* = *Proteus mirabilis*, *K. pneumonia* = *Klebsiella pneumonia*

Respiratory complications (81.4%) were most frequent during ICU stay, followed by gastrointestinal disorders (71.1%), and electrolyte imbalance (64%). Autonomic dysfunction was noted in 59% and pain in 39% of the patients [Table 10].

The mean duration of ICU stay was about 4 weeks while the hospital stay was little more than 6 weeks. Twenty

**Table 8: Management of patients**

Management	Number (%) of patients
Specific	
Plasmapheresis	17 (28.8)
IVIG	36 (61.0)
Methylprednisolone	15 (25.4)
Supportive	
Antibiotics	57 (96.6)
Antacid (s)	56 (94.9)
Sedation	43 (72.9)
Benzodiazepines	23 (39.0)
Opioids	1 (1.7)
Both	19 (32.2)
Nutrition	
Enteral (nasogastric)	56 (94.9)
Parenteral	1 (1.7)
Analgesics	25 (42.4)
Inotropic support	11 (18.6)
Antihypertensive(s)	22 (37.3)
Central venous cannulation	55 (93.2)

IVIG = Intravenous immunoglobulin

**Table 9: Respiratory features**

Features	Values
Ventilatory support	56 (94.9)
Intubation	56 (94.9)
Brought intubated	3 (5.1)
Following admission	51 (86.4)
Duration of ventilation (days)*	30.3±19 (5-80)
SIMV mode	13.8±11.3 (1-45)
CPAP mode	16.2±15.5 (0-67)
Tracheostomy	35 (59.3)
Brought tracheostomized	2 (3.4)
During ICU stay	33 (55.9)
Extubation	19 (32.2)
Time to intubation following onset of symptoms (days)**	6 (1-31)
Time to intubation following hospital admission (days)**	1 (0-15)
Interval between intubation and tracheostomy (days)**	18 (4-44)
Duration of plateau phase of ventilation (days)*	11.36±7 (1-45)

Values are no (%) of patients. \*Mean±SD (range), \*\*Median (range)  
SIMV = Synchronized intermittent mandatory ventilation,  
CPAP = Continuous positive airway pressure; ICU = Intensive care unit,  
SD = Standard deviation

one percentage of the patients died during the course of their illness. Rest of the patients could be discharged

**Table 10: Complications during ICU stay**

Complications	Number of patients (%)
Respiratory complications	48 (81.4)
Pneumonitis	27 (45.7)
Consolidation	5 (8.5)
Collapse	3 (5.1)
Pleural effusion	6 (10.2)
Pneumothorax	2 (3.4)
Multiple	4 (6.8)
Gastrointestinal disorders	42 (71.2)
Constipation	20 (33.9)
Loose motions	9 (15.3)
Constipation+loose motions	5 (8.5)
Gastrointestinal bleed	7 (11.9)
Others	1 (1.7)
Electrolyte imbalance	38 (64.4)
Autonomic dysfunction	35 (59.3)
Pain	23 (39)
Bed sore	10 (16.9)
Deep vein thrombosis	2 (3.4)
Pulmonary embolism	2 (3.4)
Seizures	5 (8.5)
Urinary tract infection	3 (5.1)

ICU = Intensive care unit

from the hospital. Of the patients who were discharged, 34% of patients had lower limb power of four or more. Thirty-four percentage of patients were on nasogastric tube feeding because of residual bulbar weakness. Though all the patients were breathing spontaneously at the time of discharge, 46.8% of the patients were still on tracheostomy tube [Table 11].

## DISCUSSION

The present series represents a selected group of patients with GBS who were treated in a specialized neurological ICU. Although this series is a retrospective study and is limited by a long-term follow up and different specific treatments, still it reflects the experience and level of management in a tertiary health care center of India.

The mean age of the patients was 35.4 years, while the median age was 27 years with a range between 11 and 79 years. The number of males was more than the female patients. According to the epidemiological review of various studies by Alter,<sup>[4]</sup> there is age dependent increment in the incidence of GBS. However, our series does not reflect such an association. On the contrary, young adult patients were more affected than the older patients. This could be due to an increased risk

**Table 11: Course and outcome**

Variables	Values
Duration of hospital stay (days)*	45.3±32 (4-187)
Duration of ICU stay (days)*	28.6±22.3 (3-88)
Maximum motor disability (nadir)	
Grade 0 power	35 (59.3)
Grade 1 power	14 (23.7)
Grade 2 power	6 (10.2)
Grade 3 power	2 (3.4)
Time to nadir following onset of symptoms (days)**	8 (2-68)
Time to nadir following admission (days)**	1 (0-58)
Reintubation (s) following extubation	4 (6.8)
Interval between extubation and reintubation (day)**	3 (0-5)
Patients discharged from hospital	47 (79.7)
Condition at discharge	
Power	
Upper limb 4 or more	23 (48.9)
Lower limb 4 or more	16 (34.0)
Feeding	
Orally	31 (65.9)
Feeding tube	16 (34.0)
On tracheostomy tube	22 (46.8)
Patients died***	13 (21.67)
Cause of death	
Cardiac arrest	6 (10.0)
Septicemia	3 (5.0)
Respiratory	2 (3.4)
Gastrointestinal bleed	1 (1.7)
Pulmonary embolism	1 (1.7)

Values are number (%) of patients. \*Mean±SD (range), \*\*Median (range), \*\*\*Data of sixty patients. SD = Standard deviation, ICU = Intensive care unit

of infections by cytomegalovirus and *Campylobacter jejuni* in the young adulthood.<sup>[18]</sup> In a study carried out at our institute, infection by *C. jejuni* and *Mycoplasma pneumoniae* has been shown to be an important antecedent illness in patients with GBS.<sup>[19]</sup> While in the southern part of India, an antecedent and recent Japanese encephalitis virus infection has an important association with GBS.<sup>[20]</sup> In almost all series, men were more affected than women (1.5:1).<sup>[21]</sup> Similarly, our series shows that the males were more affected than female patients (2.7:1).

The variants of GBS have recently become popular.<sup>[5]</sup> We observed incidence of 62.7% of AIDP, 22% AMAN and 7% of AMSAN based on electrophysiological studies. One patient had Miller-Fisher variant of GBS based on

the triad of ophthalmoplegia, ataxia and areflexia.<sup>[22]</sup> There is wide variability in the incidence of the subtypes of GBS worldwide.<sup>[23]</sup> The incidence of AIDP in Europe and North America is about 90%, while in China it is only about 20%. The incidence of AMAN in China is 60-80%, with a very low incidence (<10%) in Europe and North America. The incidence of various variants of GBS has yet to be reported in India based on epidemiologically accurate studies.

Two-thirds of patients with GBS have an antecedent acute infectious illness, and the interval between preceding infection and the onset of GBS ranges from 1 to 3 weeks (mean 11 days).<sup>[24]</sup> A number of triggering factors have been implicated in the epidemiological studies of GBS,<sup>[4,5]</sup> with an overall association in 70% of cases. Our observations are similar as 71% of the patients have a preceding event and the median time interval between the preceding event and onset of GBS is 10 days. From our study, it is understood that various nonspecific infections are important risk factors for the development of GBS.<sup>[25-27]</sup>

The cardinal features of GBS are weakness, parasthesias and diminished/absent deep tendon reflexes.<sup>[28]</sup> The initial neurological symptoms vary from patient to patient. Limb weakness (98%) was the most common presentation, followed by dyspnea (47%) and sensory symptoms (39%). Pain and sphincter disturbances were relatively less common presentation during the time of admission. Limb weakness, pain, and sensory symptoms were associated with increased median time from onset to hospital admission. However, respiratory features and sphincter disturbances necessitated early hospital admission. Hypotonia and decreased/absent reflexes were found on examination in over 90% of the patients. Most of the features are comparable to an English study on GBS patients managed in the intensive therapy unit.<sup>[11]</sup> However, our study differs from their study in a way that the sensory features were relatively less (30.5%) compared with 81% in their study. Moreover 45% of our patients had complaints of dyspnea during presentation, whereas in the English series only 5% had complaints of dyspnea. Though they do not mention the time interval from the onset of dyspnea to hospital admission, it is possible that admission was sought early in their patients that could account for the difference.

Electrolyte imbalance was noticed in 38 (64.4%) patients. Hypokalemia and hyponatremia were the most common form of electrolyte imbalance in the patients. Dyselectrolytemia appears to be multifactorial and are probably related to inadequate nutritional supplementation, metabolic and acid base imbalance and gastrointestinal disturbances.<sup>[1]</sup> Hyponatremia in patients with GBS has been attributed to the syndrome of inappropriate antidiuretic hormone.<sup>[11]</sup> Electrolyte

deficiencies were aptly restored with oral and intravenous supplementation.

The specific treatment in the patients with GBS consists of immunomodulation. Three forms of immunomodulating treatment are available for GBS—plasma exchange, high dose IVIG and corticosteroids. Plasma exchange and IVIG have been globally accepted for the treatment, while the role of corticosteroids is debatable as their use alone does not alter the outcome of GBS.<sup>[23]</sup> In a large, multicentric, randomized trial, plasma exchange (five times over 10-14 days) was compared with IVIG 400 mg/kg/day for 5 consecutive days of treatment, and with a combined treatment of plasma exchange followed by IVIG in 379 patients with severe GBS.<sup>[29]</sup> The results of the trial confirmed that plasma exchange and IVIG had equivalent efficacy, and that a combination of the two treatments was not of significant advantage. Due to the ease of administration compared with plasma exchange, IVIG is now a preferred treatment for the patients with GBS. Our retrospective series also reflects a similar trend wherein 36 (61%) patients received IVIG while only 17 (28.8%) patients received plasmapheresis. The mechanism of actions of IVIG appears to be multifactorial – modulation of complement activation products, neutralization of idiotypic antibodies, saturation of Fc receptors on macrophages and suppression of various inflammatory mediators such as cytokines, chemokines and matrix metalloproteinase.<sup>[30]</sup>

Corticosteroids are widely used to treat many autoimmune disorders. Opposed to what is expected, corticosteroids have not been shown to be of benefit in patients with GBS.<sup>[23]</sup> In a large controlled study involving 124 patients treated with high dose corticosteroids (intravenous methylprednisolone 500 mg for 5 days) and 118 patients treated with placebo, no significant difference was observed in the outcome.<sup>[31]</sup> The Cochrane evidence based review of 2006, which included six eligible trials, concluded that corticosteroids alone has no benefit in treatment of GBS.<sup>[32]</sup> Fifteen (25.4%) patients received methylprednisolone in our study. Of these, seven patients received corticosteroid in combination with either IVIG or plasma exchange. Three potentially interesting future treatments are in trial phase. They are cerebrospinal fluid filtration, interferon- $\beta$  and two new cyclooxygenase-two inhibitors.<sup>[33-35]</sup>

Supportive treatments have been subdivided into respiratory assistance and intensive care in our series. Intubation and ventilatory support were required in 56 (95%) patients. The mean duration of ventilation was 30 days. The plateau phase of ventilation was around 11 days after which most of the patients were gradually weaned off the respiratory assistance. Nineteen (32.2%) patients were extubated, while rest of the patients

was tracheostomized. When compared to a similar retrospective study, the mean duration of ventilation was less in our series (49.8 vs. 30 days).<sup>[11]</sup> However, the number of patients who required ventilation was higher in our series (94.9% vs. 73.4%). This was because the primary indication for admission to ICU in our series was ventilatory failure while in their study causes such as bulbar weakness, autonomic, and general medical factors were also considered for ICU admission. It is probable that the intensity of illness was more severe in the patients admitted to our ICU.

The development of respiratory insufficiency in GBS is due to respiratory muscle weakness that may be exacerbated by pulmonary aspiration due to impaired swallowing, and a reduced or absent cough reflex. Ventilatory support was initiated in an event of hypoxemia or hypercarbia. Intubation was generally achieved with the use of intravenous thiopentone or propofol. Sedation was used in 43 (72.9%) patients. Benzodiazepines (midazolam, diazepam) alone or in combination of opioids (fentanyl, morphine) were commonly used.

Intensive care management included the use of antibiotics in nearly all the ventilated patients. The indications for their use were fever, purulent secretions, radiographic changes or significant bacterial growth on culture. Prolonged stay in the ICU is stressful and predisposes to formation of gastric ulcers. This is aggravated with use of various medications. Consequently antacids were used in most of the patients. All the patients who had ventilatory impairment also developed bulbar weakness. Enteral feeding was initially withheld for few days and then commenced with the help of an appropriately sized feeding tube in 56 (94.9%) patients. One patient had protracted ileus and was given parenteral nutrition. The patients received regular chest and limb physiotherapy. Subcutaneous low molecular weight heparin was given to prevent deep vein thrombosis. Air mattress and intermittent change in position was advocated to avoid bed sore formation. In patients with facial weakness, eye care was given to prevent corneal ulceration.

Prolonged ICU stay has its own array of complications. Respiratory affections were seen as the forerunner, with gastrointestinal disturbances being the second. Respiratory complications were seen in as high as 81% of the patients. Although the figures are high, but it is expected as most of the patients were severely affected and the mean duration of ventilation was 30 days. Pneumonitis occurred in 27 (45.7%) patients, which in several cases was due to aspiration from oropharyngeal muscle weakness. Tracheal cultures yielded growth in almost 23 (39%) patients, the most common being

*P. aeruginosa* and *Acinetobacter* strains. Urinary tract infection was found in 16 (27.1%) patients. Growth of organism on urine culture was found in 13 (22%) of patients, the major risk factors being the use of urinary catheters in bed bound patients.

Pneumothorax occurred in two patients, one of them being a complication of subclavian route of central venous cannulation. Other patient probably had ventilator-associated pneumothorax. Chest tube was inserted in both patients with adequate lung expansion. Among the gastrointestinal disorders, constipation was the most frequent complaint. Delayed gastric emptying and ileus secondary to autonomic dysfunction are the factors implicated for the occurrence of constipation.<sup>[11]</sup> Gastrointestinal bleeding was found in seven (11.9%) patients. One patient had deranged prothrombin time, which was corrected with infusion of fresh frozen plasma. Bleeding from the ulcer sites appears to be the most probable reason for the gastrointestinal bleeding. Use of nonsteroidal antiinflammatory drugs (NSAIDs), steroids and heparin prophylaxis for deep venous thrombosis (DVT) appears to contribute to the genesis of bleeding diathesis. Though bleeding was well-controlled in most cases, one patient died of severe bleeding and shock.

Autonomic dysfunction rivals respiratory failure and thromboembolism as an important cause of death in patients with GBS. The neuropathy may involve visceral afferent fibers subserving the autonomic nervous system, parasympathetic efferent fibers, sympathetic efferents or a combination of these territories.<sup>[36]</sup> Severe paroxysmal hypertension, orthostatic hypotension and various cardiac arrhythmias are all complications that may prove difficult to manage.<sup>[37]</sup> Dysautonomia was seen in 35 (59.3%) patients. These figures are slightly less compared with a series of 169 patients with GBS at Massachusetts General Hospital where 65% had some evidence of autonomic dysfunction.<sup>[38]</sup> Mild dysautonomia such as persistent sinus tachycardia was extremely common. Antihypertensive medications were used in 22 (37.3%) patients, of which 6 (10.2%) patients already had past history of hypertension. Hypotension was treated with intravenous fluids. Inotropic support was required in 11 (18.5%) patients. 5 (8.5%) patients died following cardiac arrest due to autonomic dysfunction.

One life-threatening complication in patients with GBS is pulmonary embolism. About 5% of immobilized GBS patients have pulmonary embolism, typically after the second week of immobilization.<sup>[5]</sup> Two patients in our series had documented evidence of DVT despite the use of subcutaneous heparin and limb physiotherapy. One patient subsequently died because of pulmonary embolism. A nonlife threatening complication of GBS



that requires special attention is pain. Pain in GBS may be related to pressure areas.<sup>[39]</sup> It is managed with frequent changes in position, NSAIDs and narcotics.<sup>[39,40]</sup> Antidepressants may be used as an adjuvant to manage sleep disturbances, parasthetic pain and emotional consequences of the illness.<sup>[41]</sup> Twenty three (39%) patients complained of pain. Most of them received a combination of analgesics and antidepressants. Two patients received analgesics for nonspecific reasons. Despite adequate precautions, 10 (16.9%) patients had bed sores. All of them were adequately managed with positioning of the patient, regular dressing of sores and topical antibiotics. One complication that is unknown in GBS patients and was found in 5 (8.5%) patients was the occurrence of seizures. None of these patients had hyponatremia or hypoglycemia. One patient had history of convulsions, while no obvious reasons could correlate to the occurrence of seizures in rest of the patients. The outcome of the patients with GBS has been variably reported in different series of patients managed in specialized ICUs. Overall the mortality rates in the ICUs have been reported to be 15-20% based on various studies.<sup>[5]</sup> The patients in whom mechanical ventilation is required the mortality rates may reach 15-30%.<sup>[42,43]</sup> In our series, mortality was seen in 13 (21.7%) patients, which is similar to the world wide incidence seen in GBS patients admitted to ICU. Remaining of 47 (79.7%) patients were discharged from the hospital. Of the patients who were discharged, 16 (34%) were able to walk with or without assistance. 31 (65%) were able to swallow and were having their food orally. Less than half of the patients still required tracheostomy tube for respiration. Our incidence of mortality is much higher compared to a large series of GBS patients managed in the ICU.<sup>[11]</sup> They reported death of 4 (5%) patients. The median duration of ICU and hospital stay in their study was 19 and 33 days, while in our series it was 22.5 and 39 days respectively. The number of patients who were mechanically ventilated were higher in our series of patients (94.9% vs. 73.4%). Considering the fact that the duration of ICU stay and the number of ventilated patients were more in our series, it is possible that the severity of illness was more in our patients, resulting in greater mortality. Though the median time to nadir from the onset of symptoms was almost similar in the two studies, the number of patients who had disability grade 5 (requiring ventilatory assistance) in their study were (68.4%), while in our study it was 94.9%. This reflects greater severity of illness in our patients.

Mechanical ventilation in GBS is an indication of poor prognosis.<sup>[44-46]</sup> The need for prolonged ventilatory support was associated with increased risk of permanent disability and death in several series.<sup>[16,47]</sup> Myocardial infarction and cardiac arrest are significant causes of mortality in patients with GBS.<sup>[48]</sup> Almost, 95% of the patients required

mechanical ventilation with mean duration of 30.3 days. Consequently high mortality was present.

This study has limitations of its own. The study is retrospective in nature and consequently the data collected is based on the patient files. Fifteen files of the patients were missing during the study period, which can have an impact on the overall data, which is a drawback of this study.

Our series is a descriptive representation of severely affected patients of GBS. The study presents a comprehensive data of clinical presentation along with the course, complications and outcome in this group of patients. This study indicates that despite intensive care management of the patients with advanced form of GBS, the mortality and morbidity remains high.

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